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Profiling of seasonal variation in and cancer risk assessment of benzo(a)pyrene and heavy metals in drinking water from Kirkuk city, Iraq

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Abstract

The Lesser Zap River is the main tributary of the Tigris and is used as a main source of drinking water in Kirkuk city through the General Kirkuk project. Water samples at 13 sites were analyzed for heavy metals (cobalt, lead, manganese, copper) and benzo(a)pyrene using 2 methods of analysis (high-performance liquid chromatography (HPLC) and enzyme-linked immunosorbent assay (ELISA) kits). Risk evaluation for benzo(a)pyrene and lead in water samples was accomplished by Monte Carlo simulation.

The highest concentrations of B(a)P were recorded at sites S7 and S5, with levels of 0.192 and 0.122 $\mu\text{g L}^{-1}$ detected by HPLC and ELISA, respectively. The WHO guidelines for benzo[a]pyrene in drinking water recommend 0.0007 mg L (0.7 $\mu\text{g. L}^{-1}$), and none of the samples surpassed this level; moreover, B(a)P levels exceeded EPA standards in 2014 (0.01 ppb), particularly when the liquid-liquid extraction method with HPLC was used.

Carcinogenic risks for human adults and children exist and are highest during the rainy season as compared with the carcinogenic risk during the dry season; risks for children exceed those of adults. This indicates that the 2nd round of sampling (winter season) harbors more carcinogenic risk than the 1st round of sampling (dry season).

Key Words: Benzo(a)pyrene, heavy metals, drinking water, cancer risk, Monte Carlo simulation.

Introduction:

Aquatic pollutants mainly consist of trace elements, fertilizers, microscopic organisms, and toxic organic substances (WHO 2011; Nambatingar et al. 2017).

Heavy elements are important environmental toxic pollutants, and their toxicity is becoming more of a concern for ecological, evolutionary, nutritional, and environmental reasons (Nagajyoti et al. 2010).

36 Water pollution has direct effects on human health, while sewage and industrial effluents exert indirect
37 effects on human health through intake of foods irrigated with contaminated water. According to the World
38 Health Organization 2011, more than 80% of human diseases have origins in water. Heavy elements in surface
39 and ground water containing Mn, Cr, Fe, Cu, Ni, Cd, and Zn have negative effects on human physiology (Singh et
40 al. 2011).

41 Heavy elements can be present in trace amounts in water and are still harmful to humans and other ecosystems,
42 depending on factors such as the organisms exposed to an element, its composition, its biological function, and
43 the length of time the organisms are exposed to the element. The relationships between organisms are
44 described by food chains and food webs. Therefore, contamination of water by heavy elements affects all
45 organisms, particularly those feeding at the highest level (Lee et al. 2002). The presence of heavy elements in
46 drinking water may be related to transferred pipeline incidents.

47 These elements bind to protein sites by displacing original metals from their natural binding sites,
48 causing cell malfunction and, ultimately, toxicity. The binding of heavy elements to DNA and nuclear proteins is
49 thought to be the primary cause of oxidative degradation of biological macromolecules, according to previous
50 studies (Flora et al. 2008). Ionic oxidation stress is caused by lead toxicity in living cells. Many studies have shown
51 that oxidative stress in living cells is caused by an imbalance between the production of antioxidants to detoxify
52 or restore reactive intermediates and the production of free radicals. The ability of lead metal ions to substitute
53 for other divalent cations such as Fe^{2+} , Ca^{2+} , and Mg^{2+} , and the monovalent cation Na^+ , ultimately disturbs the
54 biological metabolism of the cell. Lead can substitute for calcium even at picomolar concentrations, affecting
55 protein kinase C, which regulates neural excitation and memory storage (Jaishankar et al. 2014).

56 PAHs in the environment consist of parent compounds and alkylated homologs. Such compounds
57 (PAHs) are of great environmental concern due to their persistence, bioaccumulation and toxic effects (Badawy
58 and Emababy 2010). The health effects of single polycyclic aromatic hydrocarbons (PAHs) may be apparent
59 under circumstances of high exposure. Long-term exposure may be more important in terms of overall public
60 health (Carpenter et al. 2002).

61 Among the sixteen PAH compounds, benzo(a)pyrene has sparked widespread interest due to its
62 carcinogenic potential and pentacyclic high-molecular-weight PAH structure. Benzo(a)pyrene and other
63 polycyclic aromatic hydrocarbons (PAHs) are widespread environmental contaminants formed by incomplete
64 combustion of organic material (IARC 2010). B(a)P has been classified by the US EPA as a probable human
65 carcinogen. There is an increase in the risk of developing cancer even at low levels, and long-term exposure
66 through drinking water is considered to represent a probable human carcinogenic risk according to the WHO
67 (2011). B(a)P should not be present at concentrations above $0.2 \mu\text{g L}^{-1}$, the maximum contaminant level (MCL).
68 Water storage tanks and distribution lines may be the major sources of B(a)P in drinking water. B(a)P in tap
69 water primarily results from the presence of PAH-containing materials in water storage and distribution systems
70 (ATSDR 1990), and the presence of PAH-containing coal tar coatings on drinking water distribution pipes and
71 storage tanks may be the primary source of B(a)P in drinking water (OEHHA 2010).

72 Health effects from overexposure to heavy metals and other chemical components in water are
73 dependent on the amount of drinking water, chemical form, age at exposure, nutritional status and lifestyle

74 (U.S. Environmental Protection Agency 2010). Copper is an essential element in human life, but chronic exposure
 75 to copper from drinking water can result in health problems such as anemia and liver and kidney damage. Even
 76 in small doses, lead can affect the central nervous system, brain, and kidneys, resulting in death or permanent
 77 damage. Manganese is an essential element for organisms and occurs naturally in many food sources. Adverse
 78 effects can result from both deficiency and overexposure (WHO 2003).

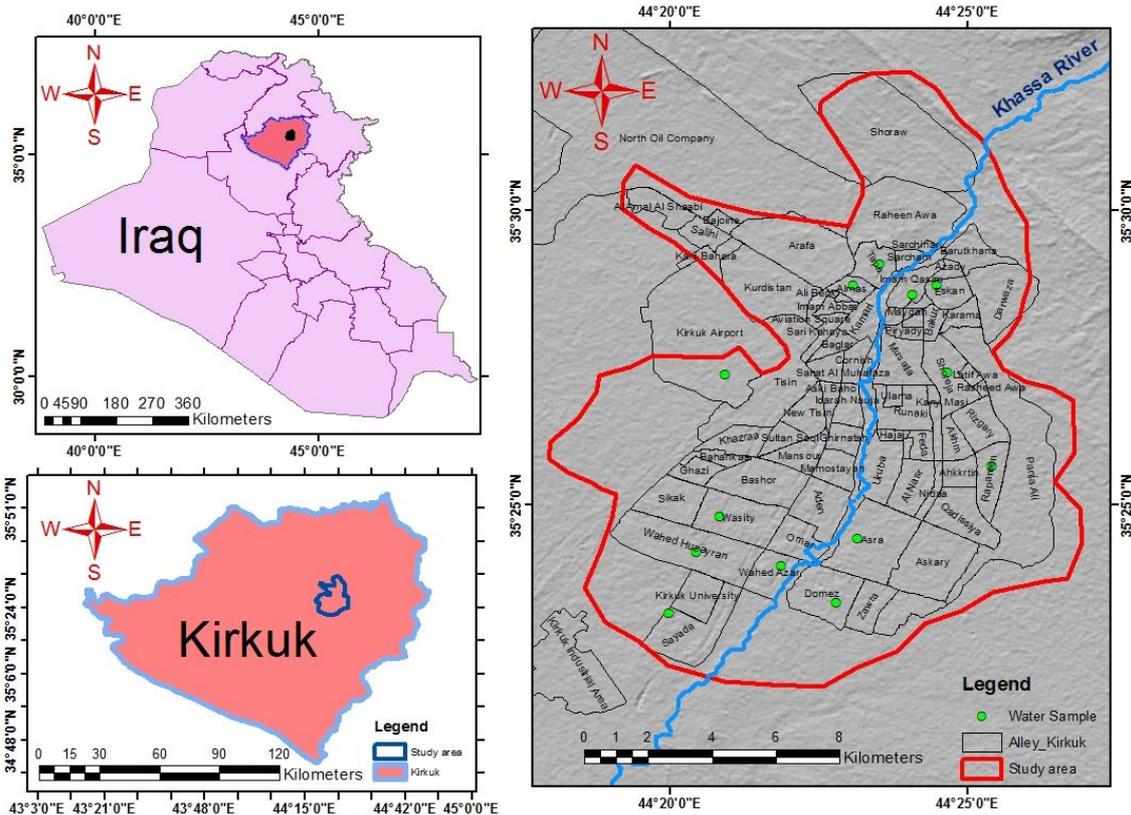
79 The main objective of this study is to provide insight into the profiles of heavy metals and
 80 benzo(a)pyrene in drinking water of Kirkuk city and produce a probabilistic cancer risk simulation with respect
 81 to human health.

82

83 **Description of the study area**

84 The Lesser Zab River originates in the Islamic Republic of Iran and is home to the Dokan Dam (6.8 km³).
 85 The river basin of 21,475 km² (of which 74 percent is in Iraqi territory) generates approximately 7.17 km³, with
 86 an annual safe yield of 5.07 km³ after construction of the Dokan Dam (OXFAM 2017). The Kirkuk drinking water
 87 treatment plant is located on the border of the Lesser Zab River at coordinates 35.67943°, 44.08357°.

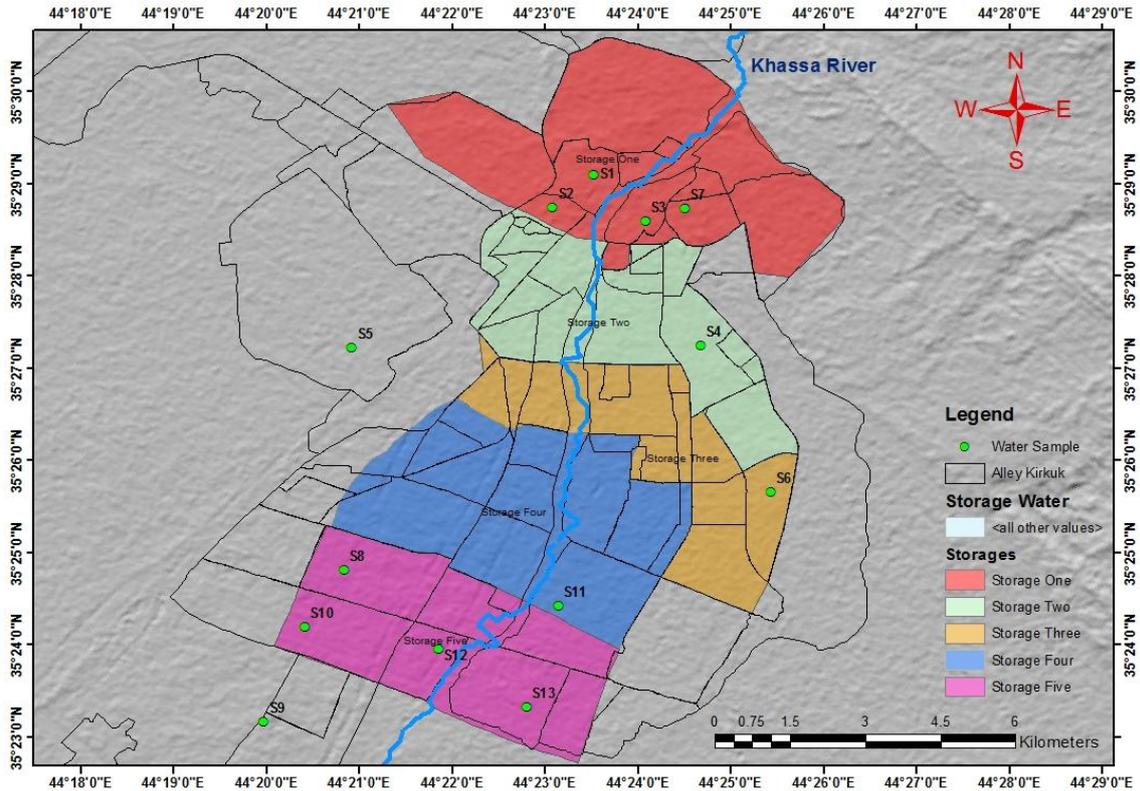
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89

90 (a)

91



92

93 (b)

94 **Fig. 1** (a) Iraq map and sampling sites in Kirkuk city and (b) water tanks ST1, ST2, ST3, ST4 and ST5 that feed all
 95 areas within Kirkuk city.

96

97 Kirkuk, the location for which this study was carried out, with an estimated population density of
 98 950,000, is one of the vital cities within northern Iraq (longitude $44^{\circ} 24'$ and latitude $35^{\circ} 28'$). Kirkuk city drains
 99 its water for drinking from the Lesser Zab River (one of the longest tributaries of the Tigris) and groundwater in
 100 some areas that have not been linked with the Kirkuk unified treatment plant. The water treatment plant in
 101 Kirkuk city includes six units: receiving well, flash mixture, clariflocculator, filters, ground tanks and high lift
 102 pumping station. After treatment, water is stored in the main storage tank (ST1) and four other storage tanks
 103 (ST2, ST3, ST4 and ST5) that feed all areas within Kirkuk city (Kirkuk Water Directorate) (OXFAM 2017). Thirteen
 104 sites within Kirkuk city were selected for collection of water samples (Fig. 1) (using clean acid-washed
 105 polyethylene bottles during June 2017 and December 2018) to prevent any problems regarding distribution
 106 networks or pipelines that transfer water to the houses (Baird et al. 2017) (Table S1).

107

108 **Material and methods**

109 **Extraction and analysis of benzo(a)pyrene in water samples**

110 The liquid–liquid extraction method described by UNEP, 1989, was used to extract B(a)P from two liters of water
 111 sample with 60 mL of CCl_4 . This step was performed twice, and the combined extracts were transferred into a
 112 flask for further preparation. Organic extracts were then evaporated to dryness by a rotary evaporator (50°C for

113 bath and 10°C temperature for water refrigerator circulator). After evaporation, the residue was dissolved in 5
114 mL acetonitrile and then concentrated to 1 mL under gentle N₂ treatment. The extract was then stored at -20°C
115 until analysis by high-performance liquid chromatography (YL9100 HPLC system) at the Ministry of Sciences and
116 Technology, Baghdad, Iraq. Approximately 12 µL of extract was injected into a capillary column of stationary
117 phase with dimensions of 15 cm×4.6 mm and then determined using a UV detector at 254 nm wavelength. Water
118 was the mobile phase, and the flow rate of acetonitrile was 1.5 mL/min. Peaks on the chromatogram were
119 identified and compared with control retention time and spectra.

120

121 **Enzyme-linked Immunosorbent Assay (ELISA) test kit Method**

122 B(a)P exists at very low levels in drinking water: to achieve high recovery, high sensitivity and high
123 reproducibility, a B(a)P ELISA test kit (MaxSignal® Benzo(a)pyrene (B(a)P) ELISA Test Kit) was used as another
124 method for measuring levels and then compared with HPLC. It is a competitive enzyme immunoassay method.
125 A 1.5 mL water sample was taken at a pH range between 6.5-7.5 and adjusted by 0.1 M HCl or NaOH. A B(a)P
126 conjugate coating was applied in the plate wells. If the target is present in the sample, it will compete for
127 antibody binding by preventing the antibody from binding to the B(a)P attached to the wells. After adding
128 substrate, the color of the secondary antibody tagged with a peroxide enzyme strengthened, and the target
129 primary antibody associated with the B(a)P coating the plate wells, resulting in an inverse relationship with the
130 target concentration in the sample. According to the Max Signal Benzo(a)pyrene ELISA test manufactured by Bio
131 Scientific, the detection limit (sensitivity) is 0.3 µ/L (ppb).

132

133 **Extraction and analysis of heavy metals**

134 For heavy metals, polyethylene containers were used for sample collection. Sampling tools and containers were
135 contamination free. Containers were washed with 10% v/v nitric acid, rinsed several times with deionized water
136 and then collected and acidified using HNO₃. Acid digestion with HNO₃ was performed as recommended by Baird
137 et al. (2017):

138 Move 100 mL of well-mixed acid-preserved sample to a flask. Supply 5 mL concentrated HNO₃ to a hood. To
139 slow boiling and evaporation on a hot plate to the smallest volume possible (approximately 10 to 20 mL) before
140 precipitation, a reflux temperature of approximately 95°C was achieved. Heating was maintained, with
141 concentrated HNO₃ added as required, until a light-colored, transparent solution emerged.

142 Digested samples were filtered using glass fiber filters and then transferred to a 100-mL volumetric flask.
143 Samples were cooled, diluted to the correct mark and mixed thoroughly. Standard solutions with different
144 concentrations of each heavy metal were prepared to obtain a standard curve according to the linear regression
145 method to obtain R²=0.997. The curve with the related parameters was plotted automatically. An AAS9000
146 Flame/Graphite Furnace Integrated Atomic Absorption Spectrophotometer of Skyray Company was employed.
147 IONEX Reference Standards from CHEM-LAB Company were used, which are certified under our ISO90001
148 Quality System and under the principles of GUM: 1995; ISO Guide 31:2000; ISO/IEC 17025. The certified value
149 for each analyzed heavy metal was 1,000 ± 4 µg/ml, and the density was ± 0.0002 g/ml. The detection limit for

150 the analyzed parameters was 0.001 mg/L. Major pollutants such as lead, manganese, copper and cobalt, were
151 analyzed in collected water samples.

152

153 **Chemicals**

154 Solvents used for extraction and analysis, such as acetonitrile, toluene, hexane, etc., were of HPLC grade and
155 were Merck and Rankem products. Standards from Sigma Aldrich (ERS 009) for 16 PAH compounds were used.
156 Silica gel with particle size 0.063 to 0.200 mm, 100 to 200 mesh ASTM from Merck was used for the current
157 work.

158

159 **Data Analysis and Mapping**

160 Data were statistically analyzed for correlation coefficients with SPSS (Version 24) with respect to
161 means of water parameters in the study area. Surfer program V16 was used for map preparation.

162

163 **Cancer Risk Assessment**

164 PAHs are natural environmental contaminants that are thought to play a role in the development of
165 human cancers. PAH compounds are metabolized enzymatically, and some of them are reactive. The CYP1A1,
166 CYP1A2, CYP1B1, and CYP3A4 cytochrome P450 enzymes are important in the metabolism of polycyclic aromatic
167 hydrocarbons (PAHs) (Walsh et al. 2013). PAHs undergo metabolic activation to diol-epoxides, which bind
168 covalently to DNA. The DNA binding of activated PAHs is essential for the carcinogenic effect (Tarantini et al.
169 2011) and has been discovered in a variety of human tissues. A strong association between epidemiological
170 studies has found a connection between PAH exposure and the number of PAH-DNA adducts (Jedrychowski et
171 al. 2013).

172 For human exposure to chemicals (PAHs and heavy metals) in drinking water by way of overt ingestion and
173 dermal absorption, the exposure dose through the ingestion pathway was measured and calculated by Equation
174 1, adapted from Exhibits 1-3, USEPA (2001),

175

$$176 \quad CDI = \frac{C_w \times IR \times EF \times ED \times CF}{BW \times AT} \quad \text{[Equation 1]}$$

177

178 where CDI stands for chronic daily ingestion of chemicals (mg kg⁻¹ d⁻¹), C_w stands for chemical concentration in
179 water (mg L⁻¹), IR stands for ingestion rate of water (L day⁻¹), EF stands for exposure frequency, 350 days year⁻¹,
180 ED stands for exposure period (year), CF stands for conversion factor (1, 10⁶ kg mg⁻¹), BW stands for body
181 weight in (kg), and AT stands for average time (day), 25,550 da.

182 The exposure dose of B(a)P through the dermal uptake pathway during bathing was calculated through
183 Equations 2 and 3, which were obtained from 'Dermal Absorbed Dose per event for Organic Compounds - Water
184 Contact', US EPA (2004).

185

$$186 \quad DA_{event} = 2FA \times K_p \times C_w \sqrt{\frac{6t_{event} \times t_{event}}{\pi}} \quad \{\text{provided } t_{event} \leq t^*\} \quad \text{[Equation 2]}$$

187

188 Where DA_{event} stands for dermal absorbed dose of B(a)P per event ($mg\ cm^{-2}\text{-event}$), FA is the fraction absorbed
189 water (dimensionless; for B(a)P, FA=1), K_p represents the dermal permeability coefficient of B(a)P, the predicted
190 value of K_p for B(a)P from the US EPA (2011) is $0.70\ (cm\ h^{-1})$, τ_{event} denotes the lag time per event ($h\ event^{-1}$), for
191 B(a)P, $\tau_{event}=2.69\ h\ event^{-1}$, t_{event} is the event duration, exposure time for shower and bathing (adults: 0.25 h/day;
192 children: 0.33 h/day) is $h\ event^{-1}$, and t^* is the time to reach steady-state (hr) = $2.4\ \tau_{event}$.

193

$$194\ DAD = \frac{DA_{event} \times SA \times EV \times EF \times ED \times CF}{BW \times AT} \quad [Equation\ 3]$$

195

196 DAD denotes daily chemical exposure via the dermal absorption pathway ($mg\ kg^{-1}\ d^{-1}$), SA denotes exposed skin
197 region in cm^2 , and EV denotes event frequency (1 bath per day; $event\ day^{-1}$).

198 The total carcinogenic risk for B(a)P present in consumed water for drinking is calculated by Equation 4:

199

$$200\ R_c = (CDI \times SF_i) + (DAD \times SF_d) \quad [Equation\ 4]$$

201

202 where R_c is the probability of developing cancer over a lifetime because of exposure to B(a)P, SF_i is the ingestion
203 cancer slope factor of B(a)P ($mg\ kg^{-1}\ d^{-1}$), which is expressed as the oral administrative dose, and SF_d is the
204 dermal cancer slope factor for B(a)P ($mg\ kg^{-1}\ d^{-1}$). All parameter values collected from citations are provided in
205 Supplementary Table S2.

206

207 In the case of heavy metals, we used the 'Dermal Absorbed Dose Per Event for Inorganic Compounds – Water
208 Contact' formula from the US EPA (2004). In this case,

209

$$210\ DA_{event} = K_p \times C_w \times t_{event} \quad [Equation\ 5]$$

211

212 The rest of the formulation for heavy metals is the same as that for B(a)P. The cancer slope factor for lead is
213 $8.5 \times 10^{-3}\ mg\ kg^{-1}\ d^{-1}$ for ingestion and $0.073\ mg\ kg^{-1}\ d^{-1}$ for dermal absorption (Mukherjee et al. 2020). K_p of lead
214 is $0.13 \times 10^{-3}\ cm\ h^{-1}$ (USEPA 2004). The rest of the detected heavy metals are not immediately carcinogenic and
215 do not have well-defined cancer slope factor values (IRIS and US EPA 1988; MDH 2020; US EPA 2008).

216 To assess which probability density functions have the greatest impact on the risk estimates, a sensitivity analysis
217 was performed using Spearman rank order correlations. Oracle's Crystal Ball (11.1.2.4.600) program was used
218 to complete the evaluation and sensitivity analysis. The same software created the 90 percent certainty
219 dimension of risk evaluation. To ensure numerical stability, a total of 50,000 iterations were considered (Tarafdar
220 et al. 2020). While the simulation is running, Crystal Ball determines sensitivity by calculating rank connection
221 coefficients between each assumption and each prediction. Correlation coefficients show how often
222 expectations and predictions are altered when they are combined.

223

224 **Results and discussion**

225 Samples from 13 sites inside Kirkuk city were collected for B(a)P and heavy metal analysis during the
 226 winter and summer seasons. The samples were tested for B(a)P, copper, lead, manganese and cobalt. The results
 227 and their concentrations in drinking water were compared with WHO guidelines for drinking purposes. The mean
 228 concentrations of all examined metals in the water assessed were not within acceptable limits (WHO 2011),
 229 posing a number of health risks.

230

231 **B(a)P in Drinking water**

232 The levels of B(a)P in the studied water samples were analyzed (Table 1 and Fig. 2 (a-d)) and showed
 233 seasonal fluctuations during the summer and winter seasons. B(a)P, a carcinogenic PAH listed as a priority
 234 pollutant by the US EPA, was detected and ranged from 0.001 to 0.192 $\mu\text{g L}^{-1}$ and 0.001 to 0.162 $\mu\text{g L}^{-1}$ as
 235 measured by HPLC and ELISA methods, respectively. A significant correlation ($P \leq 0.01$) was found between the
 236 two methods for B(a)P levels in drinking water samples; moreover, a significant correlation coefficient ($P \leq 0.01$)
 237 was found between B(a)P measured by HPLC with Cu, Co, Pb and between B(a)P measured by ELISA kit with Co
 238 only, which indicates that HPLC is more sensitive for B(a)P measurement in drinking water.

239 B(a)P levels were found to be high during the winter season compared with the summer season. Total
 240 means of 0.012 $\mu\text{g L}^{-1}$ and 0.0469 $\mu\text{g L}^{-1}$ were measured during the summer and winter seasons, respectively,
 241 when the ELISA method was used, while mean values of 0.01914 $\mu\text{g L}^{-1}$ and 0.08585 $\mu\text{g L}^{-1}$ were recorded during
 242 the summer and winter seasons when the HPLC method was used. The highest mean levels were found in the
 243 liquid-liquid extraction method with HPLC during both seasons, which indicates the greater sensitivity of the
 244 method.

245 The statistical analysis indicated that there were significant correlations ($p \leq 0.01$) between B(a)P levels
 246 between sampling sites (S2, S3, S7, S10, and S8) for the ELISA method and (S8, S2, S7, S3, S11, S10, S13) for the
 247 HPLC method and the 1st sampling time. The highest correlation numbers were found between B(a)P levels with
 248 the HPLC method and sampling sites.

249 The highest concentrations of B(a)P were recorded at sites S7 and S5, with levels of 0.192 and 0.122 $\mu\text{g L}^{-1}$
 250 L^{-1} for HPLC and ELISA methods, respectively. The guideline value of WHO for benzo(a)pyrene in water used for
 251 drinking is 0.0007 mg L^{-1} (0.7 $\mu\text{g L}^{-1}$), and none of the samples surpassed this level; moreover, B(a)P levels
 252 exceeded the EPA limit in 2011 (0.01 ppb), particularly when the liquid-liquid extraction method with HPLC was
 253 used (Table 1).

254

255 **Table 1** Benzo(a)pyrene mean levels in water samples ($\mu\text{g L}^{-1}$) at the studied sites as determined by the liquid-
 256 liquid extraction method and ELISA method.

site	B(a)P by liquid-liquid method ($\mu\text{g L}^{-1}$)		B(a)P by immunoassay (ELISA) method ($\mu\text{g L}^{-1}$)	
	Summer	Winter	Summer	Winter
1	0.014	0.06	0.009	0.024
2	0.004	0.047	0.003	0.005
3	0.007	0.017	0.005	0.01

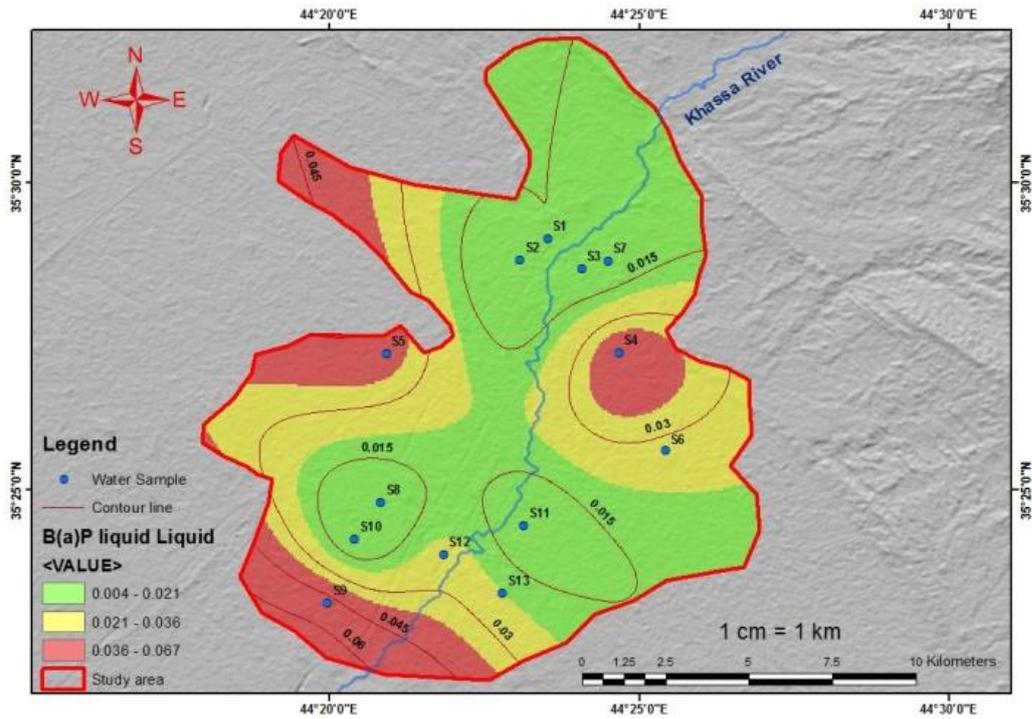
4	0.043	0.048	0.018	0.013
5	0.041	0.135	0.021	0.161
6	0.027	0.066	0.042	0.075
7	0.006	0.146	0.003	0.058
8	0.008	0.13	0.003	0.027
9	0.049	0.151	0.025	0.085
10	0.007	0.104	0.007	0.038
11	0.01	0.077	0.008	0.042
12	0.024	0.121	0.01	0.044
13	0.021	0.064	0.009	0.038

257

258 The recorded levels of B(a)P in the current study were lower than the levels recorded by Itodo et al.
 259 2018 (14.68 $\mu\text{g L}^{-1}$) in water systems in Nigeria and the results obtained by Chen 2004 (0.18–0.35 $\mu\text{g L}^{-1}$) in the
 260 Cheng-Ching Lake of Taiwan and by Chen 2007, with a value of 0.156 $\mu\text{g L}^{-1}$ for household drinking water in
 261 Taiwan.

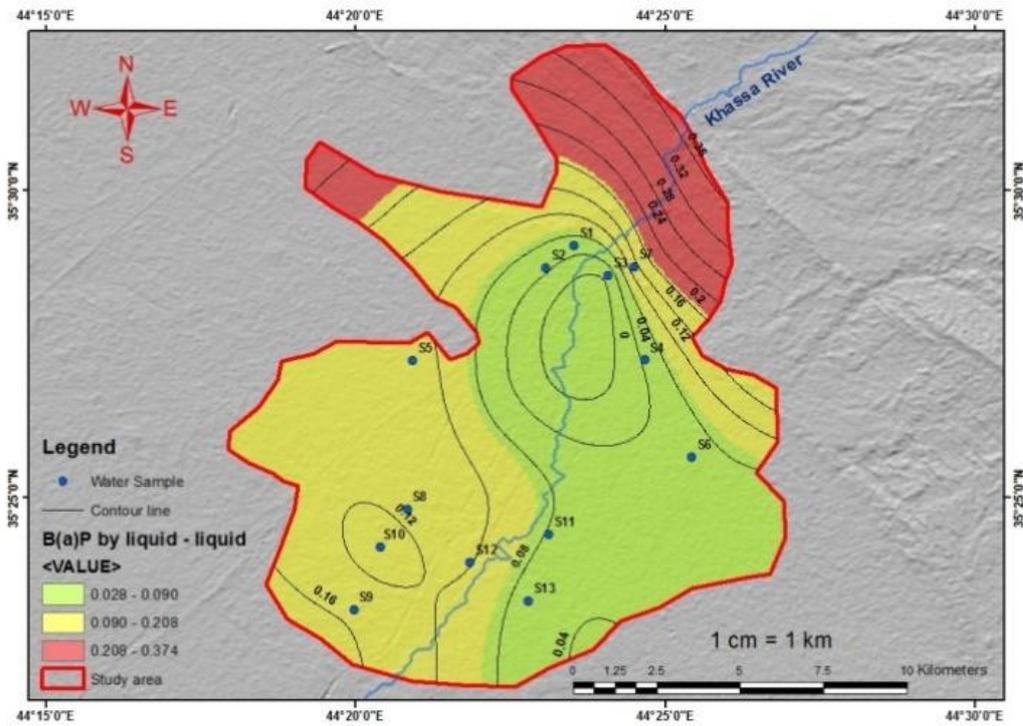
262 Because of its close association with soil, there is little knowledge regarding B(a)P concentrations in
 263 groundwater, and B(a)P is not supposed to leach into groundwater. Between 2002 and 2012, 97.6% of the 6,678
 264 samples collected in distribution networks in Québec were below the detection level (range of 0.002 – 0.01 μg
 265 L^{-1}). The median value for the studied water was 0.004 $\mu\text{g L}^{-1}$, with 20 results above 0.01 $\mu\text{g L}^{-1}$. All results were
 266 below 0.01 $\mu\text{g L}^{-1}$ in Nova Scotia (MDL 0.009 – 0.01 $\mu\text{g L}^{-1}$) (FPTCDW 2015). Badawy and Emababy (2010)
 267 concluded that none of the drinking water samples of Egypt contain any B(a)P. Similar results were obtained by
 268 Mohammed et al. 2010 in drinking water of Ifraz water treatment plants of Erbil-Iraq.

269 High levels of benzo(a)pyrene can cause skin, lung, and bladder cancer in humans and animals, making
 270 it a likely cancer-causing agent (FPTC 2015). According to the International Agency for Research on Cancer (IARC),
 271 there is enough evidence to suggest that B(a)P is carcinogenic in laboratory animals and could be carcinogenic
 272 in humans, with the ability to cause cancer in experimental animals, as mentioned by Rajendran et al. (2013,
 273 2014), due to the capability of B(a)P to induce tumors (Rajendran et al. 2008).



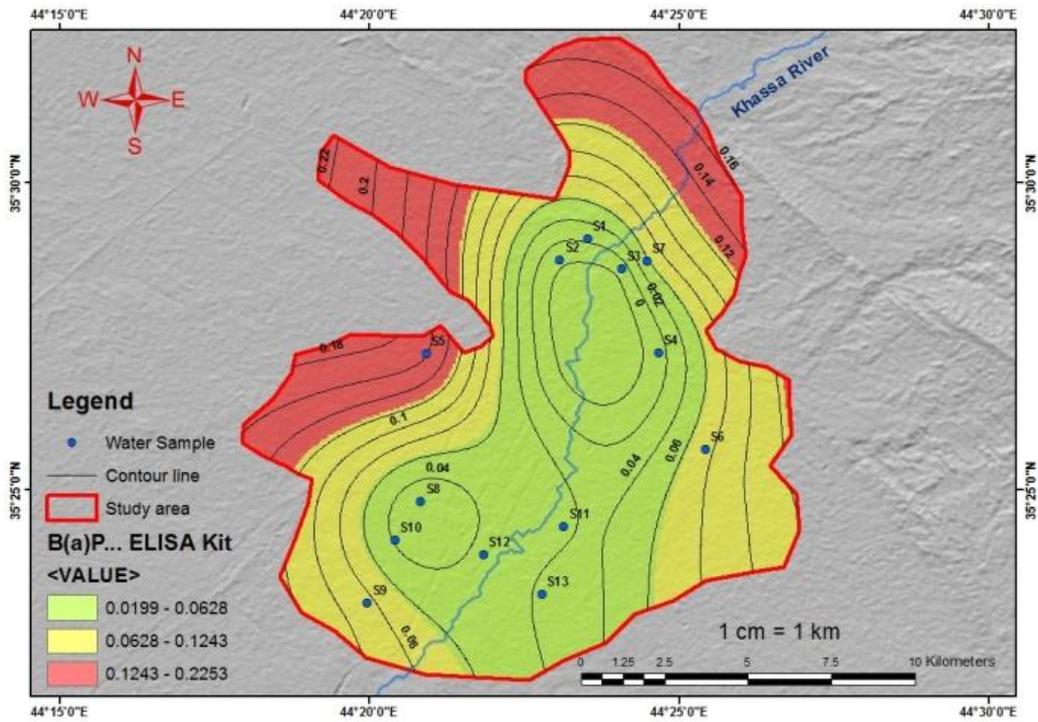
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275 (a)



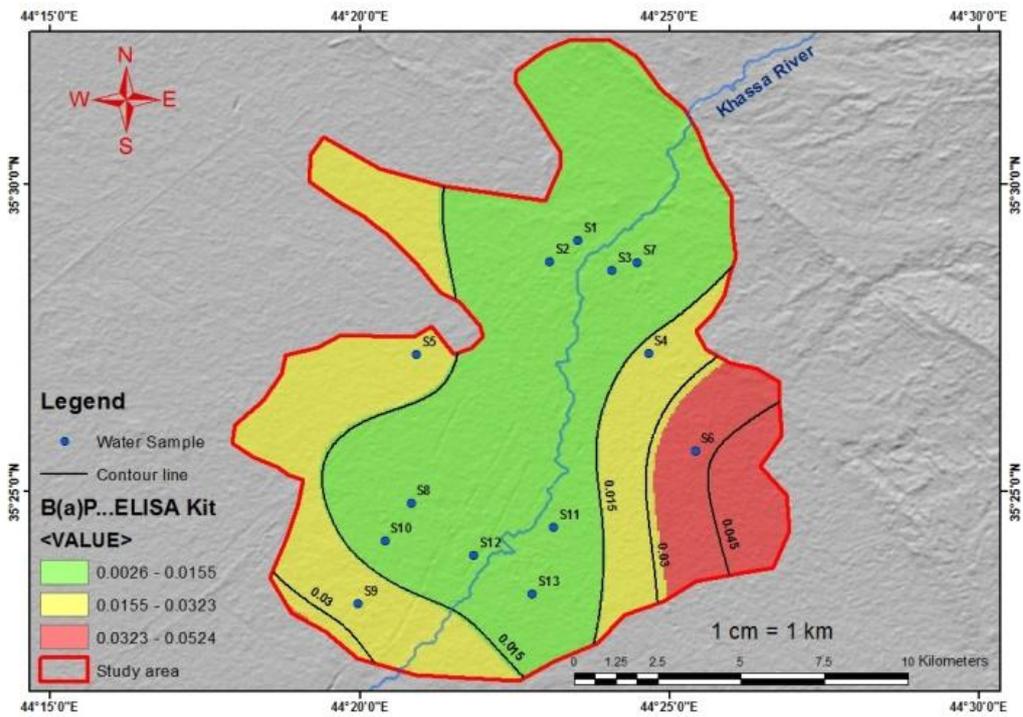
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277 (b)



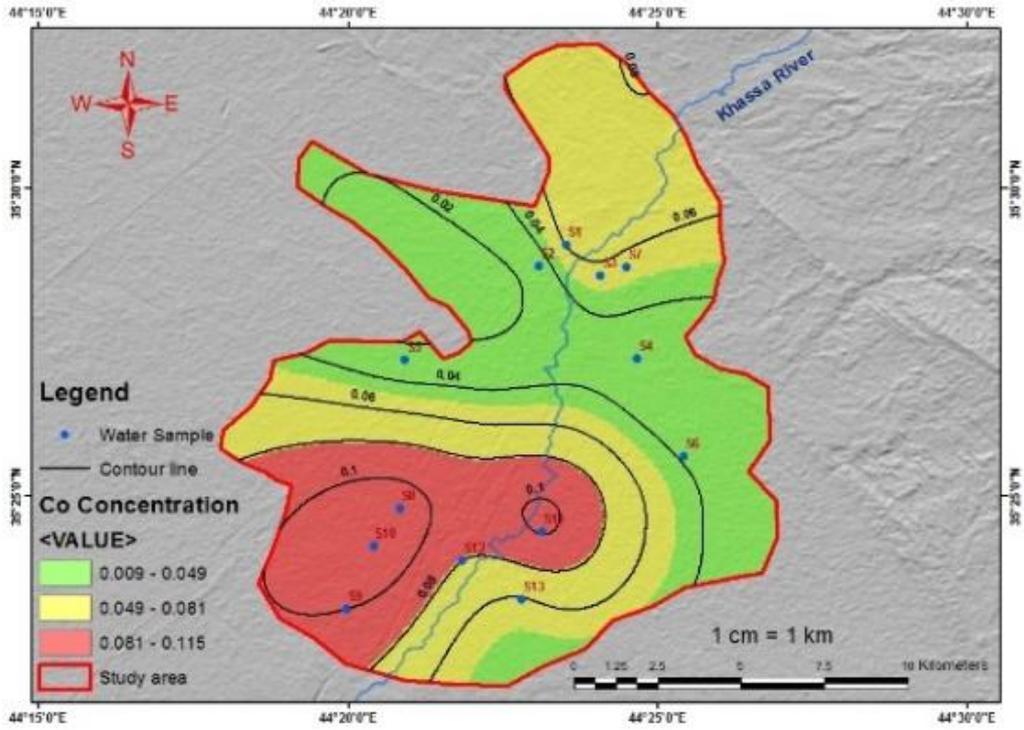
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279 (c)



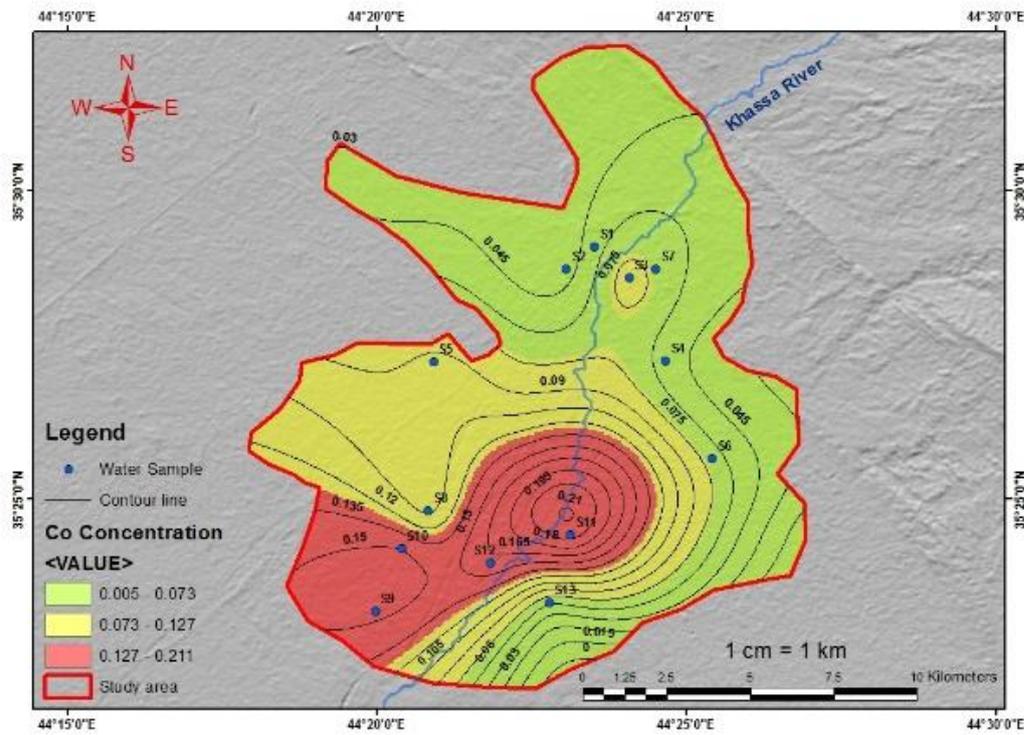
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281 (d)

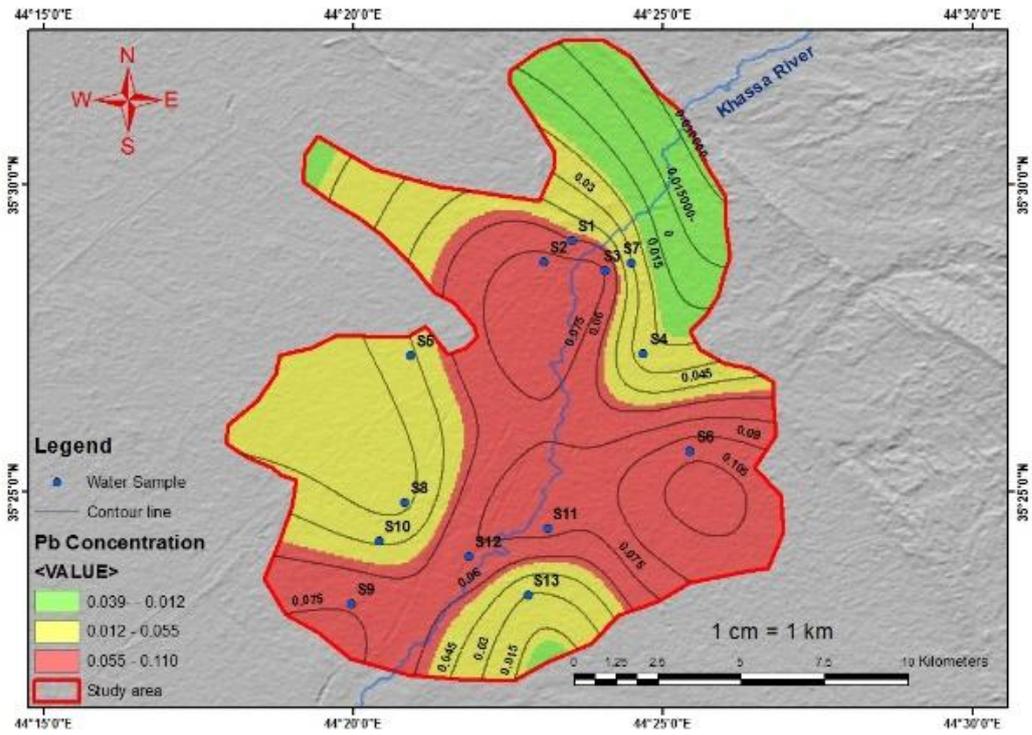


274

295 (e)

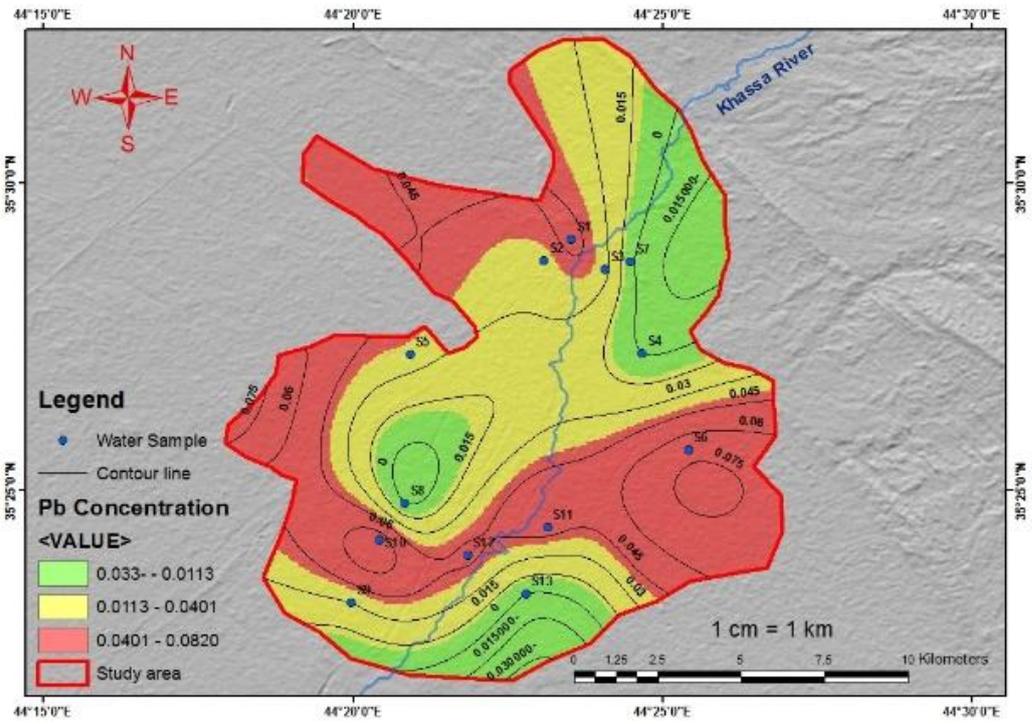


296
297 (f)



298

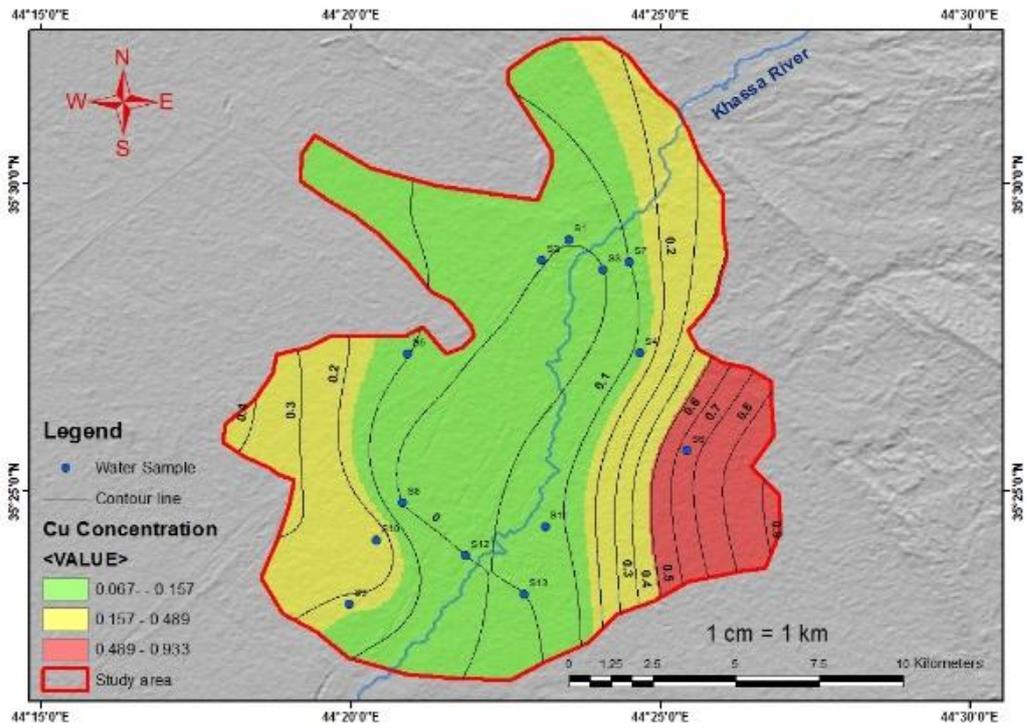
299 (g)



300

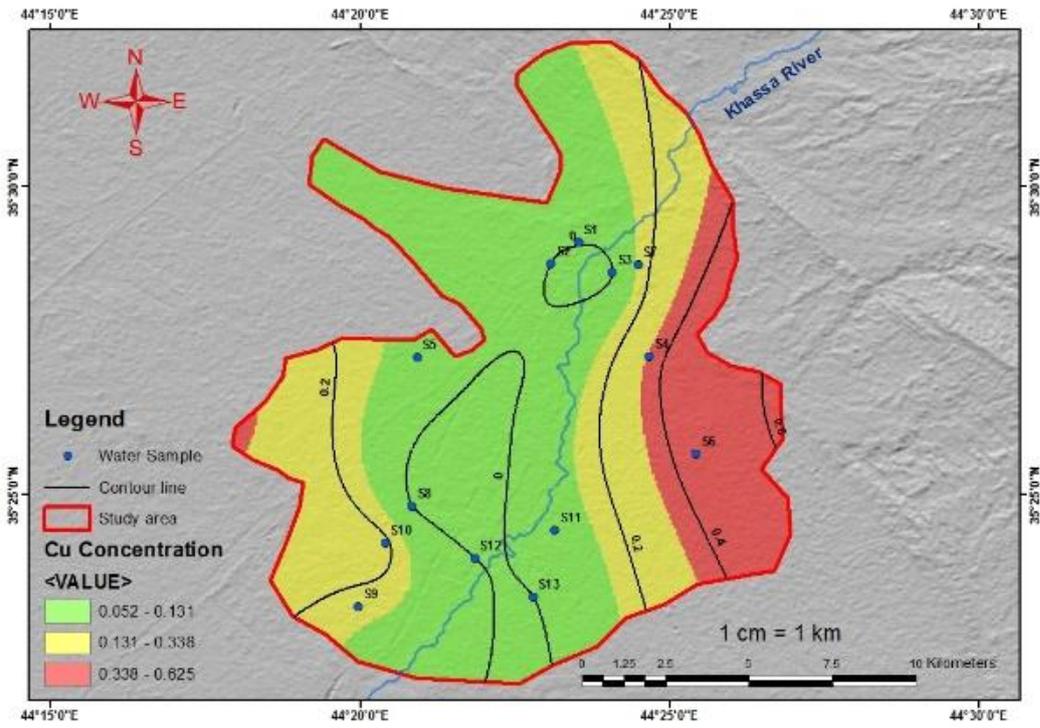
301 (h)

302



303

304 (i)

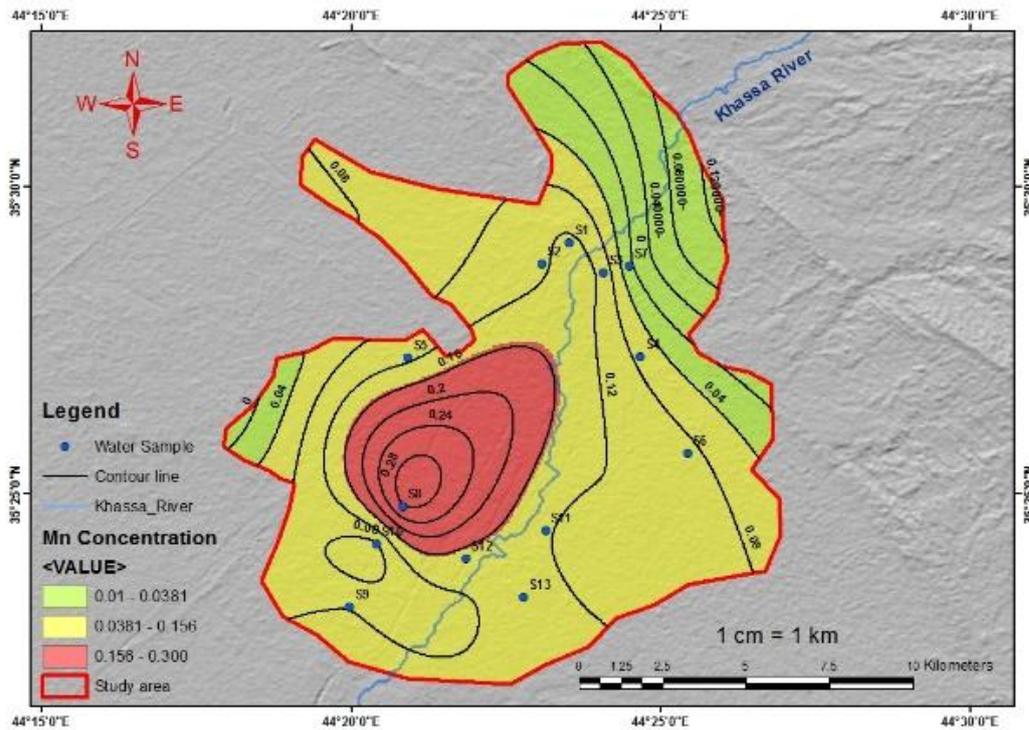


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306 (j)

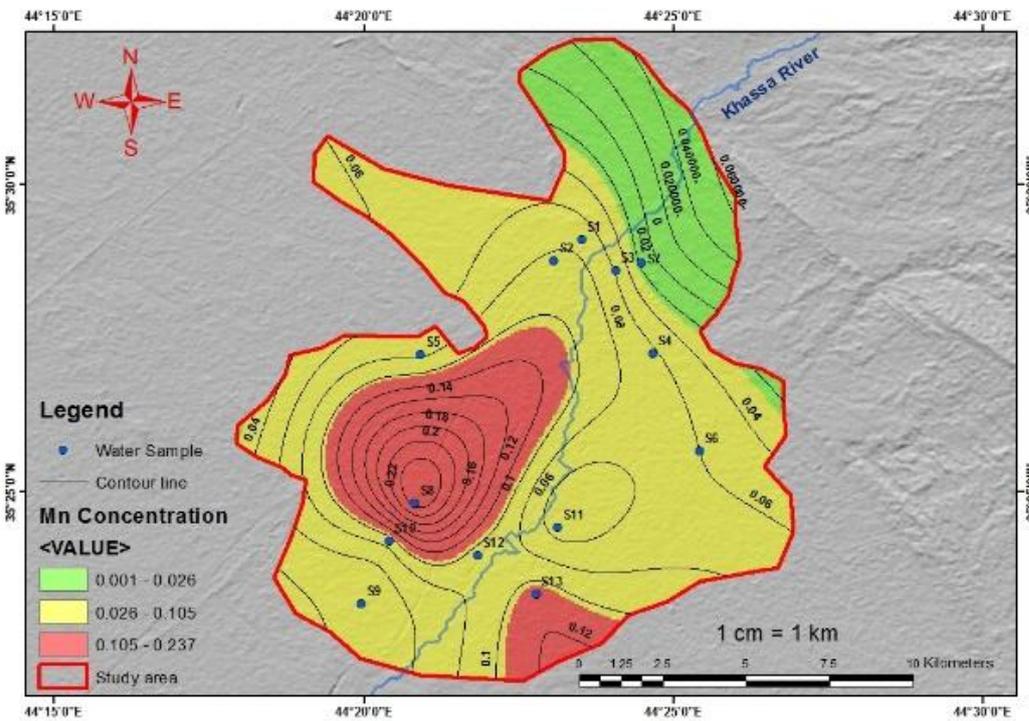
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308



309

310 (k)



311

312 (l)

313 **Fig. 2** Seasonal variation in (a-d) benzo(a)pyrene concentration determined by (a and b) liquid-liquid extraction
 314 and (b and c) ELISA, where (a and c) correspond with wet and (b and d) with dry seasons. (e and f) Cobalt
 315 concentrations during wet and dry seasons. (g and h) Lead concentrations during wet and dry seasons. (i and j)

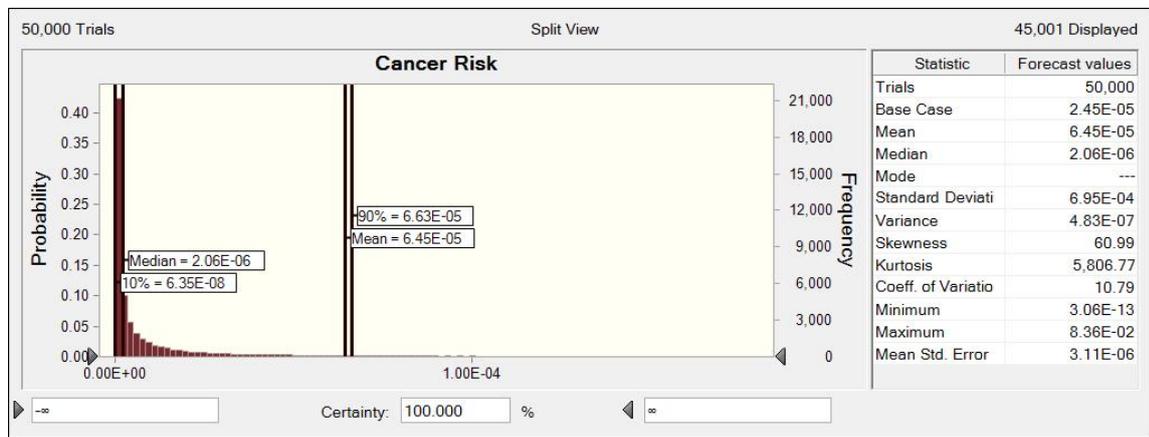
316 Copper concentrations during wet and dry seasons. (k and l) Manganese concentrations during wet and dry
 317 seasons.

318 **Risk analysis**

319 The total B(a)P concentrations for each of the samples were calculated. The geometric mean concentration of
 320 B(a)P in drinking water is (0.014, 2.300) in summer and (0.073, 1.877) in winter (geomean, geostdev in $\mu\text{g L}^{-1}$),
 321 as determined by the liquid-liquid extraction method. For the ELISA extraction method, these concentrations
 322 were (0.008, 2.296) in summer and (0.034, 2.465) in winter (geomean, geostdev in $\mu\text{g L}^{-1}$).

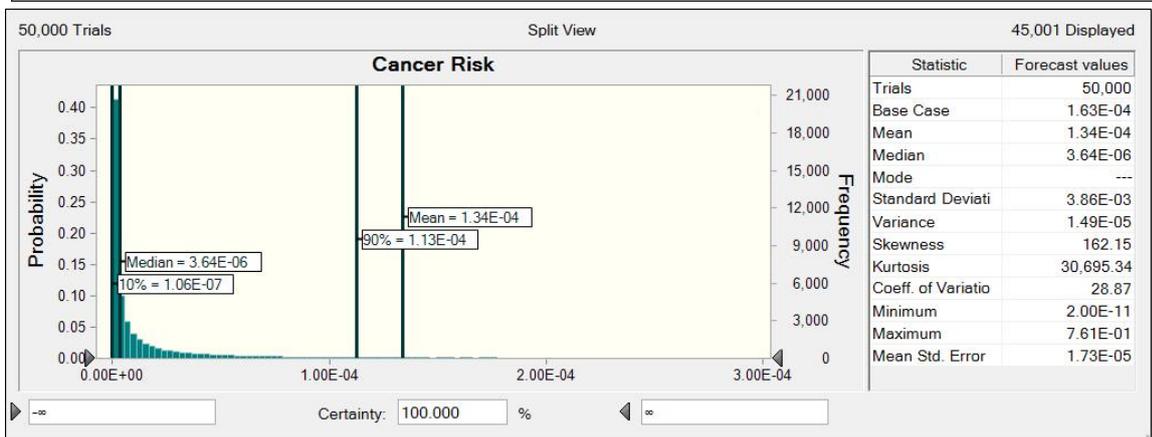
323 Bearing the different attributes of the two age groups, including ED, AF, BW, SA, EF, HR and so forth, as a primary
 324 concern, the carcinogenic hazards for children and adults were determined based on eqs. [1]-[5]. At a 90%
 325 confidence level, Monte Carlo simulation was used to evaluate risk estimation for children and adults, and the
 326 simulation results were published (for liquid-liquid extraction) and are depicted in Fig. 3. Risk simulations for
 327 ELISA extractions are depicted in Supplementary Data Fig. S1.

328



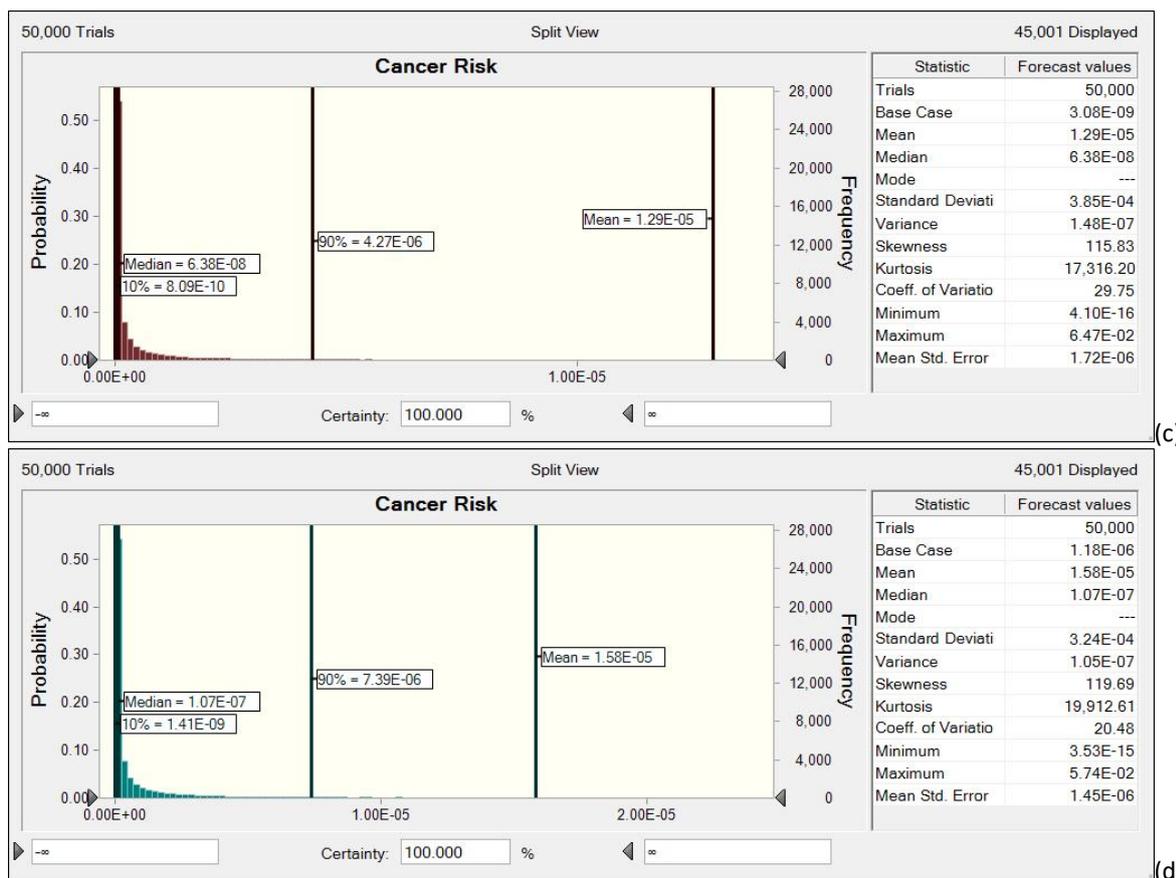
329

(a)



330

(b)



331
 332
 333 **Fig. 3** The probability density functions of cancer risk (liq-liq extraction) predicted in winter season for (a)
 334 children and (b) adults and in summer season for (c) children and (d) adults from B(a)P content of drinking water.
 335

336 According to Fig. 3, the cancer risk from drinking water was $6.35E-08$ with a mean of $6.45E-05$ for children and
 337 ranged from $1.06E-07$ to $1.13E-04$ with a mean of $1.34E-04$ for adults in the winter season, according to Monte
 338 Carlo simulation. For infants, the cancer risk from drinking water ranged from $8.09E-010$ to $7.39E-06$, with a
 339 mean of $1.29E-05$, and for adults, the risk ranged from $1.41E-09$ to $7.39E-06$, with a mean of $1.58E-05$.
 340 B(a)P was listed as carcinogenic to animals and humans by the Agency for Research on Cancer (1987) and the
 341 US Environmental Protection Agency (1984), which agreed with results obtained by Chen et al., (2020)
 342 (benzo(a)pyrene (B(a)P) > anthracene (Ant) > pyrene (Pye) > phenanthrene (Phe) > fluoranthene (Flua) >
 343 acenaphthene (Ace) > fluorene (Flu) > naphthalene (Nap).). The results of the total risk assessment in the current
 344 study had values of $4.27E-06$ in children to $7.39E-06$ in adults during the wet season and $6.63E-05$ and $1.13E-04$
 345 in children and adults during the dry season (for results obtained by the HPLC method), with a total mean of
 346 $4.77E-05$, which agreed with the results obtained by Yan et al. 2018 in southern China with a level of $2 * 10^{-5}$
 347 and the results obtained by Karyab et al. (2016) in Tehran, Iran, with a mean value of $8.81 * 10^{-05}$, and were lower
 348 than the results of Rajasekhar et al. 2018, with values of $3.76 * 10^{-3}$ in adults and $6.77 * 10^{-4}$ in children.
 349 The results of the total risk assessment in the current study include values of $4.27E-06$ in children to $7.39E-06$ in
 350 adults during the wet season and $6.63E-05$ and $1.13E-04$ in children and adults during the dry season (for results
 351 obtained by the HPLC method).

352 Moreover, lower carcinogenic risks were obtained when an ELISA kit was used, and all results for total risks (oral
353 and skin exposure) were lower, which supports our opinion that the HPLC method is more sensitive and accurate
354 for B(a)P measurement and that more variations exist between the summer and winter seasons.

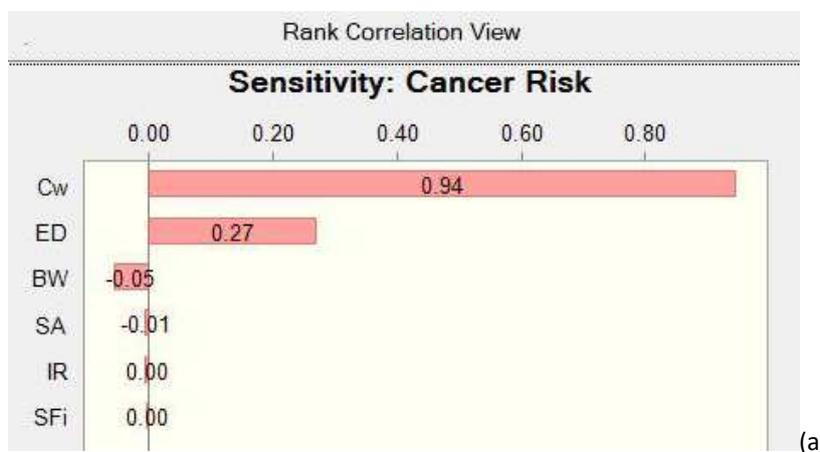
355 During both seasons, the mean values of total risk (oral and dermal) in both children and adults were found to
356 be within the US EPA permissible risk range of $1E-04$ to $1E-06$. Children were found to be at lower risk than adults
357 when subject to contamination through dermal and oral uptake because children have higher growth rates than
358 adults if compared with body weight, but the duration of exposure and ingestion rate in adults are higher: this
359 is in agreement with results of Rajasekhar et al. (2018), where adults were exposed to higher risk than children.
360 For the purpose of comparing actual risk, the US EPA established a reasonable risk of $10E-06$ (more
361 conservative). In previous studies, however, values of $10E-04$ and $10E-05$ were also considered for permissible
362 risk (Pan et al. 2015; Saha et al. 2017). The risk of direct water ingestion is found to be acceptable in both children
363 and adults when a value of $10E-04$ is used as a screening value.

364 The risk calculated from heavy metal concentration (lead) is almost negligible in comparison with the risk from
365 B(a)P. The 90% percent cancer risk for children is $2.46E-09$; for adults, the value is $3.83E-09$ in summer. In winter,
366 the 90% cancer risk for children is $5.53E-09$, and for adults, it is $9.08E-09$ in summer (Supplementary data Fig.
367 S2). These results do not heavily contribute to the total risk calculated for B(a)P. However, follow-up studies are
368 needed to determine concentrations of heavily carcinogenic heavy metals such as arsenic and cadmium.

369 According to the IARC (International Agency for Research on Cancer), there is sufficient evidence to conclude
370 that B(a)P is carcinogenic in laboratory animals and may be carcinogenic in humans, with the potential to cause
371 lung cancer in experimental animals, as stated by Rajendran et al. in 2013 and 2014 (Rajendran et al. 2008).
372 B(a)P is a carcinogenic product produced through a three-step metabolic activation process.

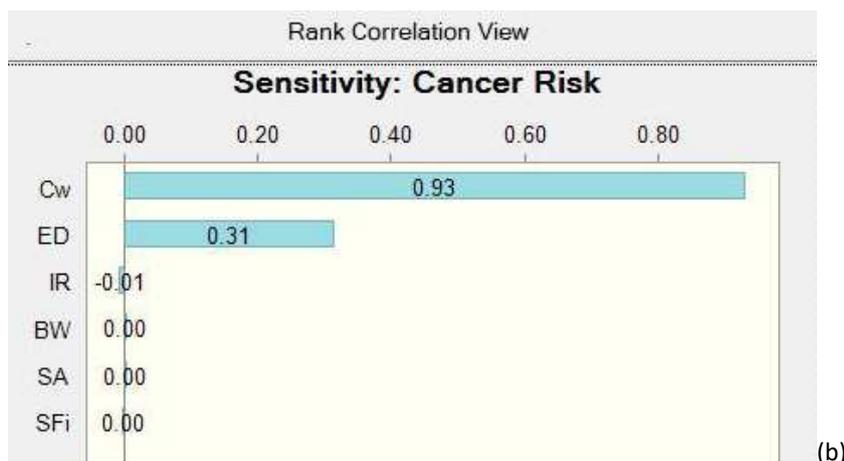
373 **Uncertainty and Sensitivity**

374 To assess the variability and ambiguity of the parameters in the risk pathway with respect to the risk assessment,
375 a quantitative analysis of the sensitivity of the risk parameters was performed. The results of the sensitivity
376 analysis of cancer risk assessment are presented as tornado plots, which depict the Spearman rank order
377 correlation coefficients on a rank scale (Fig. 4).



378

379



380

(b)

381

382 **Fig. 4** Sensitivity analysis of cancer risk parameters in two groups: children (a) and adults (b).

383

384 Variations in B(a)P (Cw) concentrations in various sampling sites appear to contribute the most to variation in
 385 overall cancer risk, followed by exposure length (ED). The key cause for consistently higher cancer risks in adults
 386 is ED, which is 11 years for children and 52 years for adults. ED is followed by body weight (BW) for children and
 387 ingestion rate of water (IR) for adults. This result is consistent with previous studies (Tarafdar et al. 2018;
 388 Tarafdar and Sinha 2017a). The accuracy of the evaluation can be improved by using a more accurate and well-
 389 defined probability distribution of ED, IR, and BW.

390 Uncertainties/vulnerabilities in health hazard assessments are unavoidable due to a lack of appropriate
 391 knowledge regarding the investigation's boundaries (Tarafdar and Sinha 2018a). However, we have utilized
 392 Monte Carlo simulation to limit vulnerability, although some of it still exists in the risk evaluation measure
 393 (Tarafdar and Sinha, 2017b, 2018b). The probable exposure parameters for water ingestion rate (IR), skin surface
 394 area (SA) and body weight (BW) were directly calculated from US EPA suggested values. These probably will not
 395 be a precise match to the Iraqi situation, making them uncertain parameters of the investigation. Precise studies
 396 are also needed for more refined definitions of the parameters identified by sensitivity analysis.

397

398 **Heavy metals in drinking water**

399 Cobalt concentrations throughout the entire study period ranged between 0.01 and 0.28 mg L⁻¹, with a
 400 total mean value of 0.0817 mg L⁻¹. The lowest value of Co (0.01 mg L⁻¹) was recorded at site 2 during the winter
 401 season, while the maximum value (0.28 mg L⁻¹) was recorded at site 12 during the winter season (Table 2). The
 402 Co results indicated that there was a significant correlation between Co and Pb and B(a)P for the studied water
 403 samples in Kirkuk city. These similarities show that the geological structure and composition of rocks represent
 404 the sources of heavy metals and govern chemical parameters in water samples (Issa and Alshatteri 2018).

405 The results of the current study were higher than the results obtained by Malkani et al. 2019 for ground
 406 water systems in India, with levels ranging between 0.128 and 0.159 ppb.

407 The cobalt concentration was found to be above the US EPA (2008) guideline (0.1 mg L⁻¹) at 3 sites
 408 during the summer season and 4 sites during the winter season, with mean values ranging from 0.027 to 0.114

409 and 0.04 to 0.2 mg L⁻¹, respectively. Twenty-one percent and 28% of sampling sites during the summer and
410 winter seasons, respectively, did not comply with the US EPA guidelines (0.1 mg L) for the maximum admissible
411 limits of cobalt in drinking water (Table 2).

412 Data for lead concentration showed significant differences ($P \leq 0.05$) with Cu and Co and with B(a)P ($P \leq$
413 0.01) between the studied sampling sites and date of sampling, with an overall mean value of 0.04542 mg L⁻¹.
414 Lead levels ranged between 0 to 0.08 and 0.01 to 0.11 mg L⁻¹ during the summer and winter seasons,
415 respectively. The results of the current study exceed the WHO guidelines (10 µg L⁻¹) for drinking water in most
416 samples collected, although Pb levels at some sites are below detection limits and agree with results obtained
417 by Mebrahtu* and Zerabruk (2011), with values ranging between <0.005 and 1.347 mg L⁻¹. High levels of lead in
418 drinking water can permanently damage the central nervous system, brain, and kidneys (Hanaa et al. 2000).

419 During the winter season, the highest level of Pb (0.11 mg L⁻¹) was found in drinking water samples 2,
420 6, and 9, and the lowest level of BDL was found in drinking water samples 4, 8, and 13. More than 10% of the
421 samples tested contained levels of lead that exceeded the WHO (2011) guidelines, and the maximum allowable
422 level of lead in drinking water was 10 µg L⁻¹. The results of the current study agreed with those obtained by Ehi-
423 Eromosele and Okiei (2012), with levels ranging from 0.020 to 0.215 mg L⁻¹.

424 The unusually high level of lead in tap water might be due to fittings made from brass, runoff from
425 domestic use, and industrial wastes (such as improper disposal of acid lead batteries and wind-blown dust), and
426 agricultural waste might be the main source of Pb pollution in the lesser Zab River which was not removed by
427 the Kirkuk water treatment plant or picked up by weathering and leaching of lead from waste rocks dumps
428 (Rajkovic et al. 2008). The levels are affected by temperature, acidity, water hardness, the length of pipes and
429 the time that water is left to stand in the pipes (stagnation) before it is drawn off (Ehi-Eromosele and Okiei 2012):
430 moreover, lower results were obtained by Alrakabi and Ramadan (2020) in drinking water of Baghdad city, with
431 levels ranging from 0 to 0.04 mg L⁻¹, yet still higher than the WHO guideline. BDL results recorded by Issa and
432 Alshatt (2018) from drinking water systems of the Garmian area in the Kurdistan Region of Iraq were lower than
433 the results of Ibrahim et al. 2018 for surface and groundwater of Samarra City, Central Iraq, with levels ranging
434 from 0.176 to 1.133 mg L⁻¹, and those of Aleseyyed et al. (2018) on ground water systems in urban and rural
435 areas of Hamadan Province in Iran, with levels ranging from 2.636 to 40.155 ppb. Lead and its compounds can
436 be present in pipes that transport water, contaminating the water (Brochin et al. 2008). Ionic toxicity occurs
437 mainly due to the ability of lead metal ions to replace other divalent cations, such as Ca²⁺, Mg²⁺, Fe²⁺, and
438 monovalent cations, such as Na⁺, which ultimately disturbs the biological metabolism of the cell (Papanikolaou
439 2005).

440

441 The results clearly indicated that there was a significant correlation ($P \leq 0.01$) with Mn and HPLC-B(a)P
442 and ($P \leq 0.05$) with Pb. These similarities show that the geological structure and composition of rocks represent
443 the sources of heavy metals and determine chemical parameters in water samples (Issa and Alshatteri 2018).
444 Significant differences were found with respect to the first round of sampling at sites S2, S3, S12 and S13. The
445 results of the current study agreed with the WHO guideline of 2 mg/L (2000 µg. L⁻¹) and are higher than the
446 results of Hussain et al., 2017 (0.00-0.01 mg. L), Ehi-Eromosele and Okiei 2012 (0.020 to 0.120 mg. L) and Malkani

447 et al. 2019 (0.027 to 0.053 mg. L) for copper in drinking water. Levels of Cu in the current study ranged from 0
 448 to 0.88 mg.L. Copper poisoning will result in chronic anemia (Acharya et al. 2008) or death due to nervous
 449 system, liver, and kidney failure if large quantities of copper compounds are consumed (Sharma and Sharma
 450 2020).

451 The manganese results revealed a negative correlation with Cu and a positive correlation with Pb, with
 452 values of -0.008 and 0.02, respectively. At levels exceeding 0.1 mg/L, manganese in water manifests an
 453 undesirable taste in beverages and stains sanitary ware and laundry (Table 2) and accumulates deposits in the
 454 distribution system. Concentrations below 0.4 mg/L are usually acceptable to consumers according to WHO
 455 2011; moreover, a concentration of 0.2 mg/L will form a black coating on pipes. The health-based value of 0.4
 456 mg/L for manganese is lower than the acceptability threshold of 0.4 mg/L (WHO 2011). Manganese deficiency
 457 can cause serious health problems, including weak bones (osteoporosis), muscle and joint pain, and sexual
 458 dysfunction (Zofkova et al. 2017). Human exposure to higher amounts of manganese can result in severe
 459 disorders in the nervous system, and long-term exposure can cause permanent neurological effects (USEPA
 460 2004). The maximum concentration of manganese (0.38 mg L⁻¹) was less than the WHO permissible limit.
 461 Zainulabdeen (2018) concluded that the water supplied to consumers is of good quality, but the periodic
 462 distribution of water may cause damage to the distribution network.

463

464 **Table 2** Mean levels of heavy metals (Co, Pb, Cu, Mn) in water samples at studied sites during summer and winter
 465 (mg L⁻¹).

466

site	Cobalt (Co)		Lead (Pb)		Copper (Cu)		Manganese (Mn)	
	Summer	Winter	Summer	Winter	Summer	Winter	Summer	Winter
1	0.061	0.054	0.047	0.060	0.004	0.006	0.073	0.127
2	0.031	0.040	0.037	0.080	0.00	0.004	0.083	0.113
3	0.055	0.080	0.033	0.073	0.00	0.00	0.057	0.103
4	0.031	0.053	0.000	0.023	0.350	0.133	0.063	0.070
5	0.027	0.093	0.037	0.043	0.087	0.102	0.077	0.113
6	0.038	0.067	0.070	0.100	0.460	0.647	0.060	0.090
7	0.054	0.070	0.003	0.030	0.143	0.100	0.016	0.010
8	0.109	0.103	0.000	0.027	0.00	0.000	0.227	0.277
9	0.100	0.153	0.030	0.073	0.160	0.177	0.050	0.117
10	0.114	0.149	0.067	0.043	0.213	0.263	0.093	0.080
11	0.101	0.200	0.050	0.08	0.067	0.070	0.053	0.123
12	0.080	0.160	0.047	0.073	0.00	0.000	0.090	0.143
13	0.059	0.063	0.000	0.030	0.00	0.000	0.110	0.130

467

468 **Conclusion**

469 B(a)P measurement is more accurate with HPLC than ELISA kits, and detected levels were higher during the wet
470 season than during the dry season. Lower carcinogenic risks were obtained when an ELISA kit was used, and all
471 results of total risks (oral and skin exposure) were lower than those of the HPLC method. Carcinogenic risks for
472 both methods were within acceptable ranges and did not surpass standards, with the highest levels found in
473 children in comparison with adults. The most significant contributors to variation in overall cancer risk appear
474 to be fluctuations in the concentration of B(a)P (Cw) in various sampling locations, followed by exposure length
475 (ED).

476 High levels of lead were measured in the studied drinking water. The risk from heavy metal exposure (lead) is
477 almost negligible in comparison with the risk from B(a)P. This study may open the gateway to future endeavors
478 with respect to PAHs, and Iraqi drinking water is contaminated with heavy metals.

479

480 **Author Declaration**

481 **1. Research Ethics**

482 Every element of the work discussed in this manuscript that does not include human patients or animals is
483 presented within the manuscript.

484 **2. Consent for publication**

485 “Not applicable”

486 **3. Availability of data and materials**

487 All data generated or analyzed during this study are included in this published article [and its supplementary
488 information files].

489 **4. Competing Interest**

490 We would like to confirm that this publication (Profiling of seasonal variation in and cancer risk assessment of
491 benzo(a)pyrene and heavy metals in drinking water from the Kirkuk region, Iraq) is free of any known conflicts
492 of interest. This study has received no direct financial funding that could have affected its results.

493 **5. Funding**

494 We wish to confirm that there are no sources of funding for the work and that the expenses were covered by
495 the authors themselves.

496 **6. Intellectual Rights**

497 We confirm that the protection of intellectual property associated with this work has been carefully
498 considered and that there are no intellectual property impediments to publication, including publication
499 timing. As a result, we confirm that we have complied with the intellectual property policies of our respective
500 institutions.

501 **7. Authors' Contributions**

533 1. **Awaz Bahrooz Mohammed** **Awaz** 1st February 2021

Siraj Goran

534 2. **Siraj Muhammed Abdulla Goran** 1st February 2021

Abhrajyoti Tarafdar.

535 3. **Abhrajyoti Tarafdar** 21st February 2021

536

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540 Technology, Baghdad, Iraq for analysis of benzo(a)pyrene by HPLC.

541

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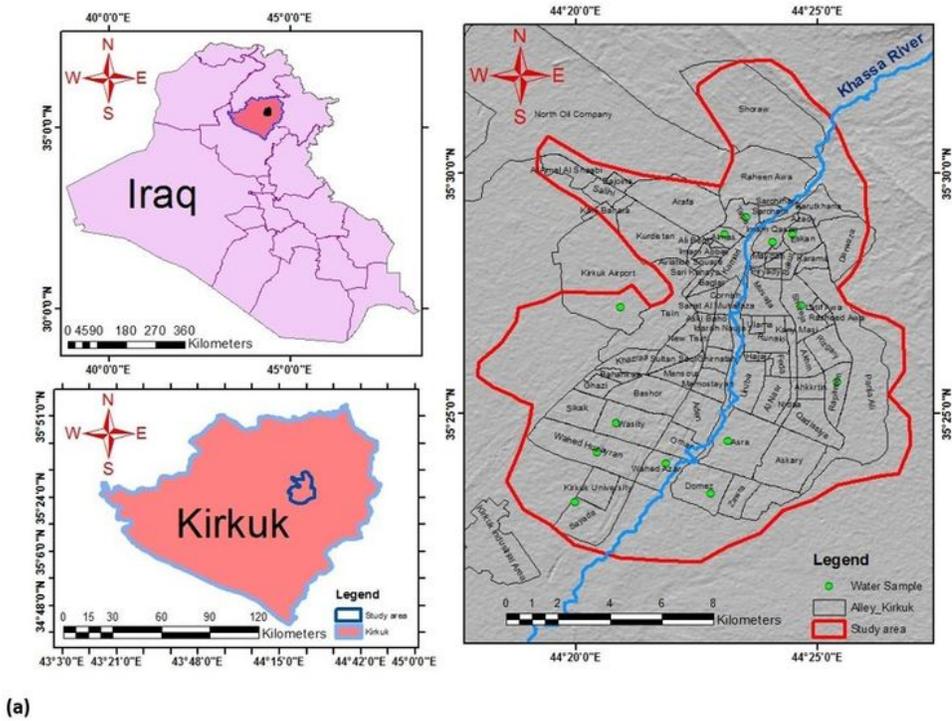
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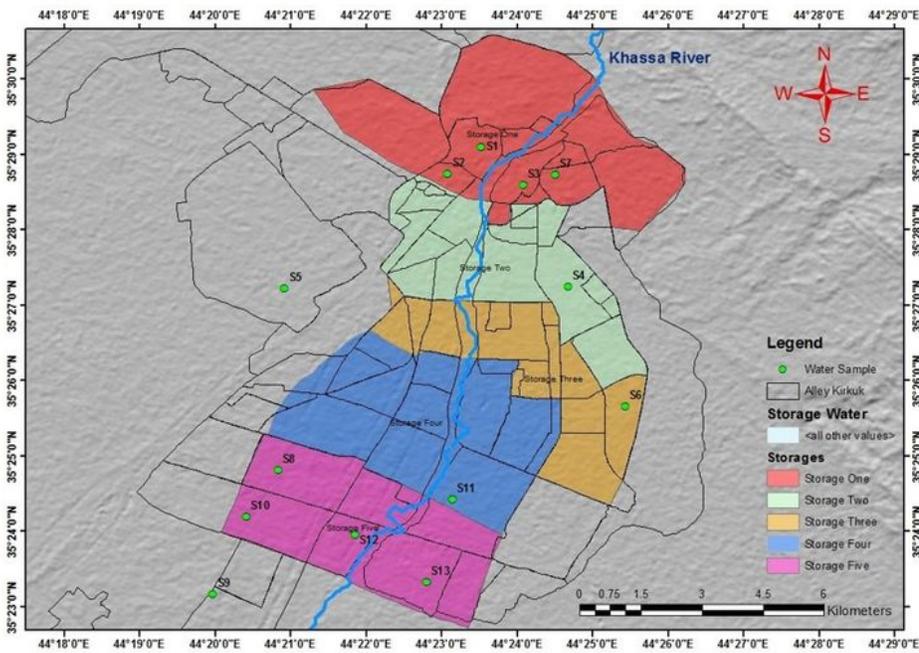
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Figures



(a)



(b)

Figure 1

(a) Iraq map and sampling sites in Kirkuk city and (b) water tanks ST1, ST2, ST3, ST4 and ST5 that feed all areas within Kirkuk city.

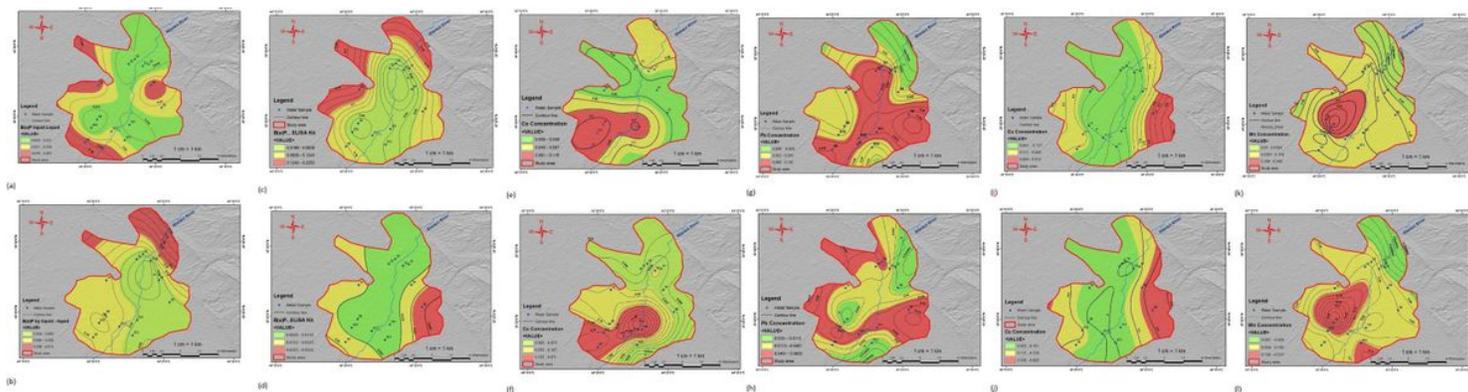


Figure 2

Seasonal variation in (a-d) benzo(a)pyrene concentration determined by (a and b) liquid-liquid extraction and (b and c) ELISA, where (a and c) correspond with wet and (b and d) with dry seasons. (e and f) Cobalt concentrations during wet and dry seasons. (g and h) Lead concentrations during wet and dry seasons. (i and j) Copper concentrations during wet and dry seasons. (k and l) Manganese concentrations during wet and dry seasons.

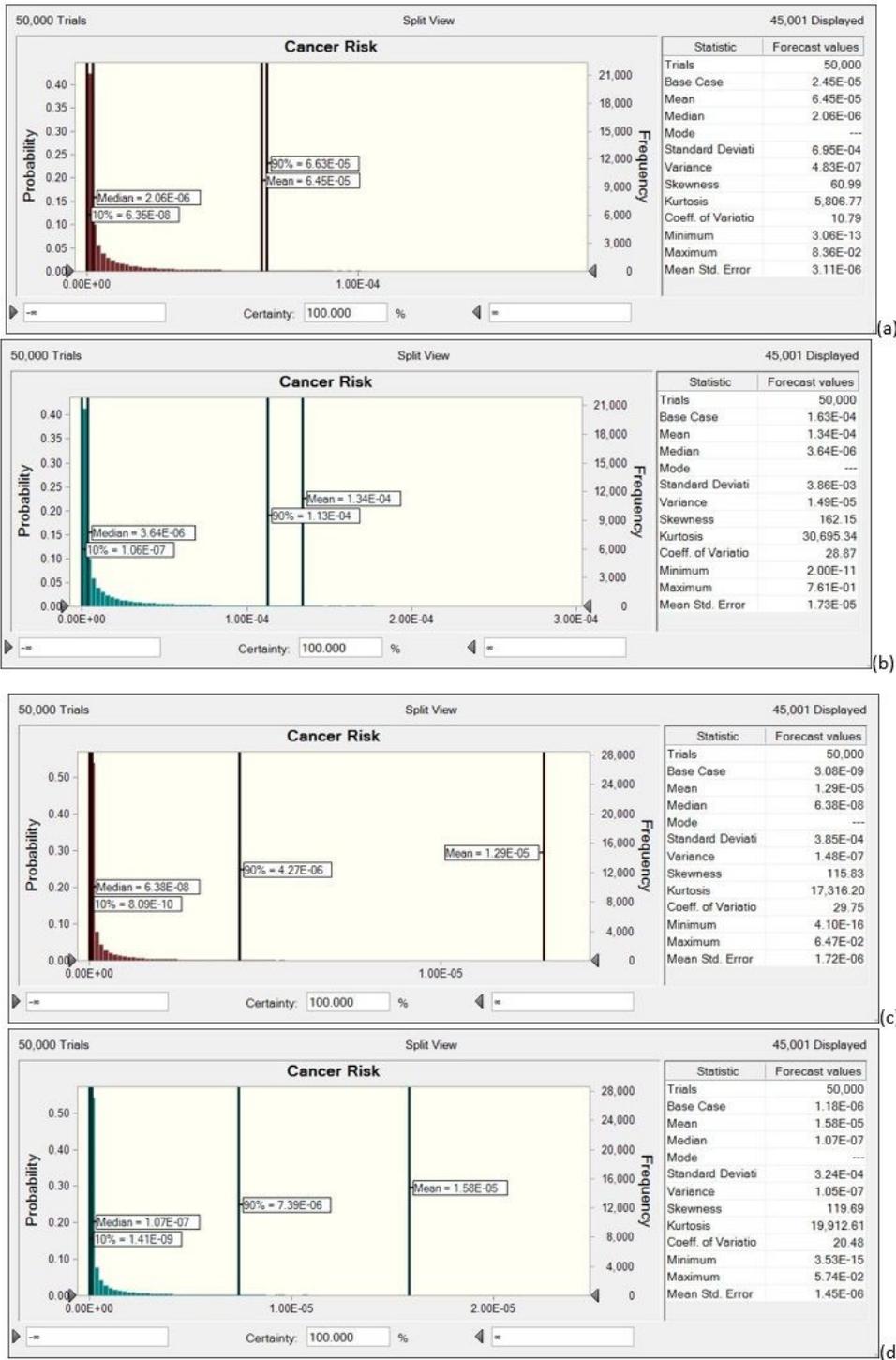


Figure 3

The probability density functions of cancer risk (liq-liq extraction) predicted in winter season for (a) children and (b) adults and in summer season for (c) children and (d) adults from B(a)P content of drinking water.

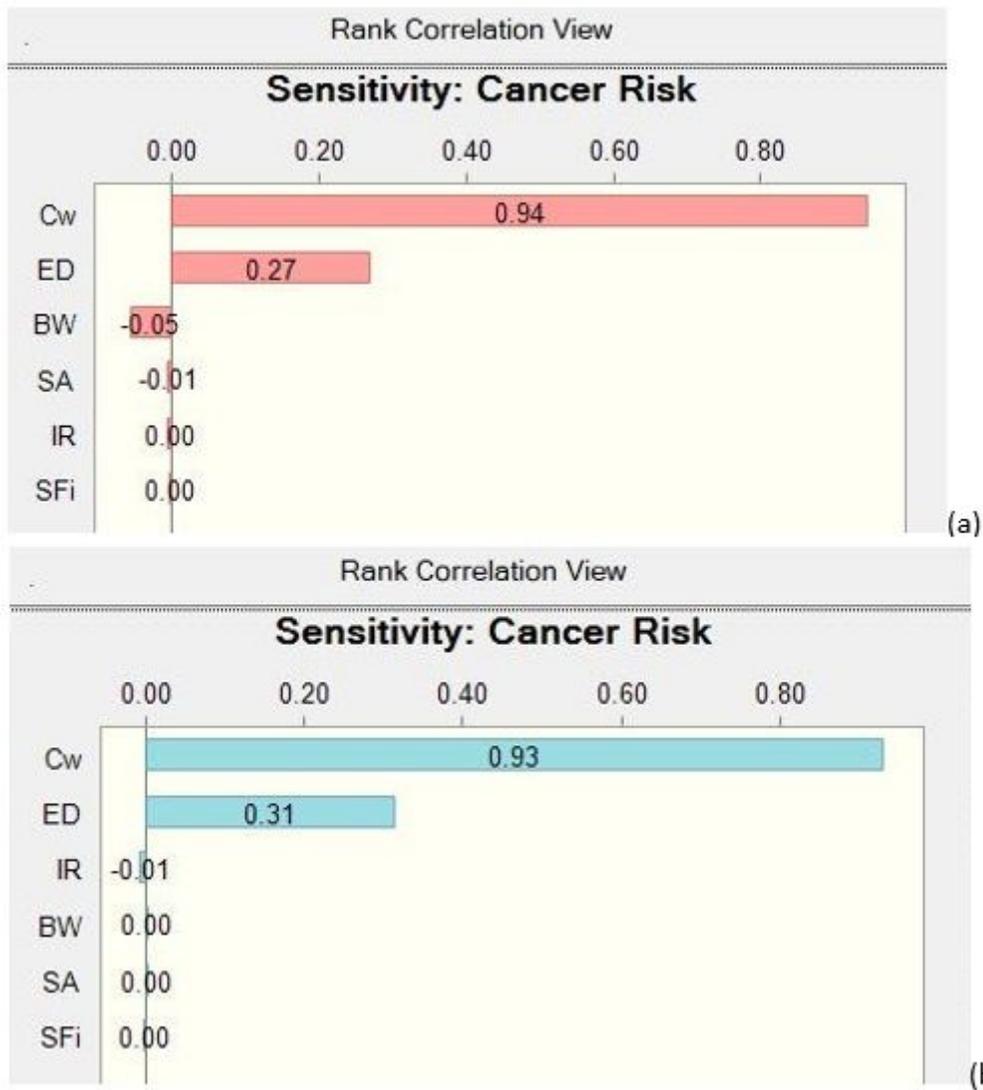


Figure 4

Sensitivity analysis of cancer risk parameters in two groups: children (a) and adults (b).

Supplementary Files

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